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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/790,562	03/01/2004	Abraham Bout	2578-4038.3US	9903
24247	7590	03/29/2006	EXAMINER	
TRASK BRITT P.O. BOX 2550 SALT LAKE CITY, UT 84110			SCHLAPKOHL, WALTER	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 03/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/790,562	BOUT ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Walter Schlapkohl	1636	<i>Waj</i>

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 February 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 11-16 and 21-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10 and 17-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>1/17/2006</u> .   | 6) <input type="checkbox"/> Other: _____                                    |

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**DETAILED ACTION**

Receipt is acknowledged of the papers filed 11/23/2005 and 2/27/2006. Claims 1-29 are pending. Claims 11-16 and 21-29 are withdrawn.

***Election/Restrictions***

Claims 11-16 and 21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/23/2005.

Newly submitted claims 22-29 are directed to an invention that is independent or distinct from the invention originally elected for the following reasons: claims 22-29 are drawn to a method for recombinant production of proteinaceous substance and would have been grouped with the non-elected Group II invention in the restriction requirement sent 11/3/2005.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 22-29 are withdrawn from

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consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicant's request for clarification of the rules regarding status identifiers for non-elected claims in light of MPEP 821 and 37 CFR §1.142(b) is acknowledged. Examiner notes that election of an invention with or without traverse and simultaneous submission of a claim set wherein non-elected claims are identified as "original" or "currently amended" is ambiguous. If the reverse had occurred, i.e. Applicant identified *elected* claims within the claim set as "withdrawn," Examiner would also treat such cases as non-responsive in order to avoid any confusion with regard to which claims are truly elected. In both situations this is done as a courtesy to Applicant *before* Examiner withdraws non-elected claims pursuant to 37 CFR §1.142(b) and MPEP 821. Therefore, the Notice of Non-compliant amendment was properly issued.

#### ***Information Disclosure Statement***

The information disclosure statements (IDS) submitted on 3/1/2004 and 5/26/2005 and 1/17/2006 are acknowledged.

The information disclosure statements filed 1/17/2006 and 5/26/2005 fail to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-

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patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. They have been placed in the application file, but the information referred to therein has not been considered as indicated by Examiner.

### ***Specification***

The disclosure is objected to because of the following informalities: the use of the trademark PER.C6™ has been noted in this application on page 9, paragraph 43, for example. It should be capitalized wherever it appears and be accompanied by the generic terminology. In this instance, the trademark/trade name is used to identify/describe a human embryonic restinoblast cell line containing Adenovirus serotype 5 (Ad5) E1A and E1B-encoding sequences under the control of the human phosphoglycerate kinase (PGK) promoter. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

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***Claim Objections***

Claims 8 and 17 are objected to because of the following informalities: claims 8 and 17 are objected to for containing the acronyms "PGK" and "CMV," respectively, which should be spelled out at their first occurrence. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 10 & 17, and therefore dependent claims 3-9 & 18-20, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 10 and 17 recite a "proteinaceous substance." Claims 1, 2, 10 and 17 are vague and indefinite in that it is unclear what the metes and bounds of a "proteinaceous substance" are. Does a proteinaceous substance include only proteins, proteins comprising non-protein components, or substances that are similar to proteins?

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Claim 10 recites "[t]he eukaryotic cell of claim 1, wherein the proteinaceous substance is a human protein" in lines 1-2.

Claim 10 is vague and indefinite in that the metes and bounds of "human protein" are unclear. Does Applicant intend that "human proteins" encompass any protein comprising a naturally-occurring human protein sequence and/or any "humanized" antibodies, or does Applicant intend a more narrow scope of proteins which naturally occur in humans?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 9 is drawn to or encompasses eukaryotic cells comprising a first nucleotide sequence encoding an adenoviral protein E1A protein, a second nucleotide sequence encoding an

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adenoviral E1B protein, and wherein the genome of the eukaryotic cell lacks a nucleotide sequence encoding a structural adenoviral protein and wherein the eukaryotic cell does not express a structural adenoviral protein, and wherein the cell comprises a recombinant nucleotide sequence in expressable format encoding a proteinaceous substance. The claim further encompasses such cells deposited under ECACC number 96022940. The application discloses a retinoblast cell line that is encompassed by the definitions for **biological material** set forth in 37 C.F.R. § 1.801. Because it is apparent that this biological material is essential for practicing the claimed invention, it must be obtainable by a reproducible method set forth in the specification or otherwise be known and readily available to the public as detailed in 37 C.F.R. §§ 1.801 through 1.809.

It is unclear whether this biological material is known and readily available to the public or that the written instructions are sufficient to reproducibly construct this biological material from starting materials known and readily available to the public. Accordingly, availability of such biological material is deemed necessary to satisfy the enablement provisions of 35 U.S.C. § 112. If this biological material is not obtainable or available, the requirements of 35 U.S.C. § 112

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may be satisfied by a deposit of the biological material. It is noted that the retinoblast cell culture (Dep. Ref. 96022940) has been accepted by the ECACC as a patent deposit in accordance with the Budapest Treaty of 1977 on February 29, 1996. However, in order for a deposit to meet all criteria set forth in 37 C.F.R. §§ 1.801-1.809, applicants or assignee must provide assurance of compliance with provisions of 37 C.F.R. §§ 1.801-1.809, in the form of a declaration or applicant's representative must provide a statement. The content of such a declaration or statement is suggested by the enclosed attachment. Because such deposit will not have been made prior to the effective filing date of the instant application, applicant is required to submit a verified statement from a person in a position to corroborate the fact, which states that the biological material which has been deposited is the biological material specifically identified in the application as filed (37 C.F.R. § 1.804). Such a statement need not be verified if the person is an agent or attorney registered to practice before the Office. Applicant is also reminded that the specification must contain reference to the deposit, including deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

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**Double Patenting**

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10 and 17-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 and 9-11 of copending Application No. 10/644,256. Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant claims are drawn to a species of the copending

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claims' genus insofar as they are drawn to a *eukaryotic* cell for producing a proteinaceous substance. The instant claims are drawn to a species of the copending claims' genus also insofar as the instant claims require that the *eukaryotic* cell lack a nucleotide sequence encoding a structural adenoviral protein in its genome and requires that the *eukaryotic* cell not express a structural adenoviral protein. The copending claims are drawn to a species of the instant claims' genus insofar as the cell of the copending claims encodes an IgA molecule whereas the claims of the instant application encompass a cell encoding for any proteinaceous substance. The copending claims are further drawn to a species of the instant claims' genus insofar as they limit the cell to one *expressing* E1A and E1B proteins of an adenovirus whereas the instant claims require only that the *eukaryotic* cell encode such proteins. It would have been obvious to utilize a *eukaryotic* cell which lacks a nucleotide sequence encoding a structural adenoviral protein in its genome and which does not express a structural adenoviral protein and which not only encodes adenoviral E1A and E1B proteins, but also expresses such proteins in the instant invention, because the copending application contains embodiments with *eukaryotic* cells such as human cells that meet these limitations (see, e.g., disclosure of the 10/622,256 application at page 6, paragraph 17). In

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addition, both sets of claims are drawn to human cells, cells derived from retina cells, cells derived from primary cells as well as cells deposited under ECACC number 96022940. Finally, both sets of claims are drawn to such cells in culture.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-10 and 17-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-19, 21-35 and 41-42 of copending Application No. 10/234,007. Although the conflicting claims are not identical, they are not patentably distinct from each other. Both sets of claims are drawn to a eukaryotic cell for producing a proteinaceous substance, said cell comprising a nucleotide sequence encoding an adenoviral E1A protein, a nucleotide sequence encoding an adenoviral E1B protein, and wherein the genome of said cell does not express a structural adenoviral protein, and wherein the cell comprises a recombinant nucleotide sequence in expressible format encoding the proteinaceous substance. The instant claims are drawn to a genus of the copending claims' species insofar as the copending claims are drawn to a eukaryotic cell for producing a protein

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comprising a variable domain of an immunoglobulin or an entire immunoglobulin as opposed to any proteinaceous substance. The instant claims are further drawn to a genus of the copending claims species insofar as the copending claims are limited to such a cell wherein the recombinant nucleotide encoding the proteinaceous substance is under the control of a heterologous promoter.

With respect to instant claims 1-10 and 17-18, an obvious-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claims(s). Although the conflicting claims are not identical, they are not patentably distinct from each other because, in the case of instant claims 1-10 and 17-18, they are generic to all that is recited in the respective claims of the copending application, i.e., the copending claims fall entirely within the scope of each of instant claims 1-10 and 17-18.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

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Claims 1-10 and 17-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 14-15 and 18-19 of copending Application No. 11/271,090. Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant claims are drawn to a eukaryotic cell encoding adenoviral E1A and E1B proteins, said cell comprising recombinant nucleic acid encoding a proteinaceous substance in expressible format. The claims are further drawn to such a cell wherein said cell is a human cell, wherein said cell is derived from a cell deposited under ECACC number 96022940, an immortalized human retina cell. The copending claims are drawn to an immortalized human retina cell expressing E1A and E1B proteins of an adenovirus, wherein said immortalized human retina cells comprise recombinant nucleic acid encoding an IgM molecule in expressible format. The copending claims are drawn a species of the instant claims' genus insofar as the copending claims are drawn to *immortalized human retina* cells comprising recombinant nucleic acid encoding a human IgM molecule, whereas the instant claims are drawn to a *eukaryotic* cell comprising recombinant nucleic acid ending any proteinaceous substance. The copending claims are also drawn to a species of the instant claims' genus insofar as the copending claims limit the cell to

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one *expressing* adenoviral E1A and E1B proteins as opposed to the instant claims which only limit the cell to one *encoding* such proteins. Both sets of claims are drawn to PER.C6 cells which lack a nucleotide sequence for a structural adenoviral protein in its genome and which does not express a structural adenoviral protein.

With respect to instant claims 1-10 and 17-18, an obvious-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claims(s). Although the conflicting claims are not identical, they are not patentably distinct from each other because, in the case of instant claims 1-10 and 17-18, they are generic to all that is recited in the respective claims of the copending application, i.e., the copending claims fall entirely within the scope of each of instant claims 1-10 and 17-18.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-10 and 17-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of copending Application No. 10/499,298. Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant claims are drawn to a cell encoding E1A and E1B proteins of an adenovirus, said cell comprising recombinant nucleic acid encoding a proteinaceous substance in expressible format. The claims are further drawn to such a cell wherein said cell is a human cell, wherein said cell is derived from a retina cell, wherein said cell is derived from a primary cell and wherein said cell is derived from a cell deposited under ECACC number 96022940. The copending claims are drawn to a host cell comprising adenovirus E1 sequences and further comprising recombinant nucleic acid encoding an immunologically active bivalent multimeric antibody fragment, and/or a precursor thereof, functionally linked to one or more sequences capable of driving expression of said fragment in said host cell. The instant claims are drawn to a species of the copending claims' genus insofar as the copending claims encompass any host cell comprising a recombinant nucleic acid encoding an immunologically active bivalent multimeric antibody fragment, and/or a precursor thereof, functionally linked to one or more

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sequences capable of driving expression of said fragment in said host cell and the instant claims are drawn to a only eukaryotic cells. The instant claims are also drawn to a species of the copending claims genus insofar as the instant claims are limited to a cell comprising nucleotide sequences encoding adenoviral E1A and E1B proteins whereas the copending claims encompass host cells comprising any adenoviral E1 sequence. The instant claims are also drawn to a species of the copending claims genus insofar as the instant claims are limited to cells which lack a structural adenoviral protein in the genome and which do not express a structural adenoviral protein.

It would have been obvious for one of ordinary skill in the art to use a eukaryotic cell which encodes both an adenoviral E1A and an adenoviral E1B protein and which lacks a nucleotide sequence encoding a structural adenoviral protein in its genome and which does not express a structural adenoviral protein, because the copending application teaches such a cell as a preferred embodiment (see references to PER.C6 cells, e.g. page 6, lines 21-32).

With respect to instant claims 1-10 and 17-18, an obvious-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference

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claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claims(s). Although the conflicting claims are not identical, they are not patentably distinct from each other because, in the case of instant claims 1-10 and 17-18, they are generic to all that is recited in the respective claims of the copending application, i.e., the copending claims fall entirely within the scope of each of instant claims 1-10 and 17-18 with the exception of the limitations which have been addressed above.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-10 and 17-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 28-29, 31-40 and 43-50 of copending Application No. 11/039,767. Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant claims are drawn to a eukaryotic cell encoding E1A and E1B proteins of an adenovirus, said cell comprising recombinant nucleic acid encoding a proteinaceous substance in expressible format. The claims are further drawn to such a cell wherein said cell is a human cell, wherein said

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cell is derived from a retina cell, wherein said cell is derived from a primary cell and wherein said cell is derived from a cell deposited under ECACC number 96022940. The claims are further drawn to such a cell in culture. The copending claims are drawn to a host cell comprising at least one exogenously introduced nucleic acid sequence encoding an immunoglobulin light chain and at least two different immunoglobulin heavy chains. The claims are further drawn to such a host cell wherein said at least one exogenously introduced nucleic acid sequence is present on a low copy number vector and said host cell produces 1-20 pg per cell per day of two or more non-identical antibodies.

The instant claims are drawn to a species of the copending claims insofar as they are drawn to a *eukaryotic* cell for producing a proteinaceous substance whereas the copending claims encompass any host cell. The instant claims are also drawn to a species of the copending claims' genus insofar as they are drawn to cells which lack a nucleotide sequence encoding a structural adenoviral protein in the genome and wherein the cell does not express a structural adenoviral protein. The instant claims are further drawn to a species of the copending claims' genus insofar as the instant claims are drawn to a cell comprising a first and second nucleotide sequence encoding an adenoviral E1A and E1B protein, respectively, whereas the copending claims have

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no such limitations. In this respect, it would have been obvious to utilize a eukaryotic cell in the instant invention with such limitations, because the copending application contains as a preferred embodiment a eukaryotic cell such as human embryonic retinoblast cell which encodes adenoviral E1 proteins and which lacks nucleic acids encoding a structural adenoviral protein in the genome (see, e.g., disclosure of the 11/039,767 application at page 8, paragraph 18; and page 71, paragraphs 197-199).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-10 and 17-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 37-39 of copending Application No. 10/497,832. Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant claims are drawn to a eukaryotic cell encoding E1A and E1B proteins of an adenovirus, said cell comprising recombinant nucleic acid encoding a proteinaceous substance in expressible format. The claims are further drawn to such a cell wherein said cell is a human cell, wherein said cell is derived

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from a retina cell, wherein said cell is derived from a primary cell and wherein said cell is derived from a cell deposited under ECACC number 96022940. The claims are further drawn to such a cell in culture. The copending claims are drawn to a human cell comprising a heterologous nucleic acid encoding an alpha sialyltransferase.

The instant claims are drawn to a genus of the copending claims species insofar as the instant claims encompass a *eukaryotic* cell comprising a recombinant nucleotide sequence whereas the copending claims are drawn to a *human* cell comprising a recombinant nucleotide sequence. The instant claims are also drawn to a genus of the instant claims' species insofar as the instant claims are drawn to a cell comprising a recombinant nucleotide sequence encoding any proteinaceous substance whereas the copending claims are drawn to a cell comprising a recombinant nucleotide sequence encoding an alpha sialyltransferase. The instant claims are also drawn to a species of the copending claims' genus insofar as the instant claims are drawn to a cell further comprising a first and second nucleotide sequence encoding adenoviral E1A and E1B proteins and wherein the genome of the cell lacks a nucleotide sequence encoding a structural adenoviral protein and wherein the *eukaryotic* cell does not express a structural adenoviral

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protein. It would have been obvious for one of ordinary skill in the art to utilize a cell with such limitations in obtaining a human cell comprising a heterologous nucleic acid encoding an alpha sialyltransferase because the copending application's disclosure uses a cell with such limitations as a preferred embodiment (see the 10/497,832 disclosure at, e.g. page 10, lines 20-32; and page 11, lines 1-15).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-10 and 17-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 42-49 of copending Application No. 11/026,518. Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant claims are drawn to a eukaryotic cell encoding E1A and E1B proteins of an adenovirus, said cell comprising recombinant nucleic acid encoding a proteinaceous substance in expressible format. The claims are further drawn to such a cell wherein said cell is a human cell, wherein said cell is derived from a retina cell, wherein said cell is derived from a primary cell and wherein said cell is derived from a cell deposited

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under ECACC number 96022940. The claims are further drawn to such a cell in culture. The copending claims are drawn an immortalized human embryonic retina cell comprising a nucleic acid sequence encoding an adenoviral E1A protein and nucleic acid sequence encoding an enzyme involved in post-translational modification of proteins, wherein said enzyme is under control of a heterologous promoter. The instant claims are drawn to a genus of the copending claims' species insofar as the copending claims are drawn to an immortalized human embryonic retina cell whereas the instant claims are drawn more broadly to any eukaryotic cell. The instant claims are drawn to a species of the copending claims' genus insofar as the instant claims encompass cells which comprise a nucleic acid sequence encoding an adenoviral E1B proteins in addition to an adenoviral E1A proteins. It would have been obvious for one of ordinary skill in the art to substitute a human embryonic cell further comprising a recombinant nucleic acid encoding an adenoviral E1B protein when obtaining the human embryonic retina cell of the copending application because the copending application teaches such a cell as a preferred embodiment (see, e.g., page 11, paragraph 37).

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-9 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Fallaux et al (WO 97/00326).

Fallaux et al teach a eukaryotic cell for producing a proteinaceous substance, said eukaryotic cell comprising a first nucleotide sequence encoding an adenoviral E1A protein; a second nucleotide sequence encoding an adenoviral E1B protein; wherein the genome of the eukaryotic cell lacks a nucleotide sequence encoding a structural adenoviral protein and wherein the eukaryotic cell does not express a structural adenoviral protein; and a recombinant nucleotide sequence in expressible format encoding the proteinaceous substance (see entire document, especially page 25, lines 21-33; page 29, lines 33-36; page 30, lines 1-2 & 32-33). The proteinaceous substances

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taught by Fallaux are beta-galactosidase and thymidine kinase (see, e.g., page 28, lines 1-9 and Figure 9). Regarding claims 3-6, Fallaux et al teach such a eukaryotic cell wherein the cell is of a human cell origin, wherein the cell is of a retina cell origin and wherein the cell is of a primary cell origin and further wherein the cell is of a human embryonic retinoblast origin (see page 29, lines 33-36). Fallaux et al further teach such a cell wherein the first and second nucleotide sequences encoding the adenoviral E1A and E1B proteins are integrated in the genome of the eukaryotic cell and are derived from nucleotides 459-3510 of an adenovirus 5 genome (page 25, lines 15-17). Fallaux et al further teach such a cell wherein the first nucleotide sequence encoding the adenoviral E1A protein is regulated by a human PGK promoter (see page 25, lines 15-17). Fallaux et al further teach such a eukaryotic cell of a PER.C6 cell origin as deposited under ECACC no. 96022940 (see page 30, lines 3-4). Regarding claim 18, Fallaux et al teach a cell culture of such a eukaryotic cell in a suitable medium (page 27, lines 20-30).

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***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10 and 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fallaux et al (cited above) in view of Dorai et al (US Patent Number 5,631,158).

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Fallaux et al teach a eukaryotic cell for producing a proteinaceous substance, said eukaryotic cell comprising: a first nucleotide sequence encoding an adenoviral E1A protein; a second nucleotide sequence encoding an adenoviral E1B protein; wherein the genome of the eukaryotic cell lacks a nucleotide sequence encoding a structural adenoviral protein and wherein the eukaryotic cell does not express a structural adenoviral protein; and a recombinant nucleotide sequence in expressible format encoding the proteinaceous substance, as described above. Fallaux et al also teach such a cell in culture in a suitable medium, also described above. Fallaux et al further teach that the PER.C6 cell line is stable for more than 57 passages (page 11, lines 7-10).

Fallaux et al do not teach such a cell wherein the recombinant nucleotide sequence in expressible format encoding the proteinaceous substance forms part of the genome of the eukaryotic cell. Fallaux et al do not teach such a cell wherein the proteinaceous substance is a human protein. Nor do Fallaux et al teach such a cell in culture, wherein the cell culture is a suspension culture, or wherein the suitable medium is free of animal- or human derived serum and animal- or human-derived serum components.

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Dorai et al teach a method for high protein production utilizing a eukaryotic cell. Dorai et al teach such a method wherein the eukaryotic cell comprises a recombinant nucleotide sequence encoding a proteinaceous substance and wherein the proteinaceous substance is a human protein (see entire document, especially column 6, lines 19-25 and lines 35-44). Note that here Examiner has interpreted "human protein" to encompass proteins comprising sequences from naturally occurring human proteins. Dorai et al also teach that the proteins to be produced can be any protein but human proteins are included as a preferred embodiment, especially such proteins in the form of sFv molecules, which "provide attractive alternatives to intact immunoglobulins and Fab fragments due to their small size and their stability at concentrations that typically promote dissociation of natural Fv fragments" (column 5, lines 48-51). Dorai et al teach that the eukaryotic host cell can be "any cell that can be immortalized, i.e. are viable for multiple passages (e.g., greater than 50 generations), without significant reduction in growth rate or protein production (column 8, lines 53-57). Dorai et al teach that the recombinant nucleotide sequence encoding the proteinaceous substance is stably integrated into the genome of the host cell (see, e.g. column 4, lines 25-27 and 52-55; and column 9, lines 37-41). Dorai et al

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also teach that the recombinant nucleotide sequence encoding the proteinaceous substance in expressible format comprises the sequence encoding the proteinaceous substance under control of a CMV promoter (see, e.g. column 8, lines 10-13; and column 13, lines 1-7). Dorai et al further teach that such promoters are preferred in situations where the transactivating protein is ElA because such viral proteins can stimulate the (viral CMV) promoter that induces transcription of the recombinant proteinaceous substance (column 8, lines 1-13). Dorai et al further teach such a eukaryotic host cell in a suitable medium wherein the suitable medium is free of animal or human-derived serum and animal-or human-derived serum components (see, e.g. column column 10, lines 15-25). Dorai et al teach that growth in serum-free media is key to realizing the benefit of the enhanced production of certain proteins of interest (ibid) and that the preferred cell line has "simple media composition requirements" (column 12, lines 54-57). Dorai et al further teach such a cell in culture, wherein the cell culture is a suspension culture (column 12, lines 55-56) and wherein the cell culture is adapted for suspension culturing as preferred embodiments (column 8, lines 60-62).

It would have been obvious for one of ordinary skill in the art to use the cells of Fallaux et al in the method of protein

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production as taught by Dorai et al, which encompasses the use of a genomically-integrated proteinaceous substance under the control of a CMV promoter and further adapting host cells to growth in serum-free media and suspension, because Dorai et al teach that their method can be practiced with any eukaryotic cell line that can be immortalized (passaged 50 times or more without significant reduction in growth rate or protein production) and Fallaux et al teach such an immortalized cell line, the PER.C6 cell.

One of ordinary skill in the art would have been motivated to combine the cells of Fallaux with the elements as taught by Dorai et al for the ability to produce high amounts of human proteins. Each element taught by Dorai, viz. the recombinant proteinaceous substance under the control of a CMV promoter, the human protein, the cells capable of or adapted to growth in serum-free media and suspension culture, has a corresponding additional motivating factor. In the case of the CMV promoter, the motivation to use such a promoter lies in the fact that expression of its operably-linked gene can be increased when E1A is used as a transactivator and the PER.C6 cells of Fallaux et al express E1A. In the case of the human protein, Dorai et al teach that such proteins as a preferred embodiment and that, in the case of the sFv molecules, are attractive candidates to the

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larger immunoglobulins and Fab fragments due to their smaller size and greater stability. Cells capable of growth in serum-free media and suspension culture, as taught by Dorai et al, are also preferred and key to the invention for large scale production purposes.

Thus, based on the teaching of the prior art, the high level of skill of one of ordinary skill in the art and absent evidence to the contrary, one of ordinary skill in the art would have had a reasonable expectation of success when combining the cells of Fallaux et al with the method and elements of Dorai et al.

#### Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is (571) 273-8300. Note: If Applicant does submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent applications to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Walter A. Schlapkohl whose telephone number is (571) 272-4439. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office.)

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.

Walter A. Schlapkohl, Ph.D.  
Patent Examiner  
Art Unit 1636

March 18, 2006

  
NANCY VOGEL  
PRIMARY EXAMINER

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## SUGGESTION FOR DEPOSIT OF BIOLOGICAL MATERIAL

## ATTACHMENT

A declaration by applicant or assignee, or a statement by applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material. Such a declaration:

1. Identifies declarant.
2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address. (See 37 C.F.R. § 1.803).
3. States that the deposited material has been accorded a specific (recited) accession number.
4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent. (See 37 C.F.R. § 1.808(a)(2)).
5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. § 1.14 and 35 U.S.C. § 122. (See 37 C.F.R. § 1.808(a)(1)).
6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer. See 37 C.F.R. § 1.806).
7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.